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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/090,827	03/06/2002	Francois Bertelli	A0000179-C1-66-MG	6882

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WARNER-LAMBERT COMPANY
2800 PLYMOUTH RD
ANN ARBOR, MI 48105

EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 10/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	10/090,827	BERTELLI ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08/30/3004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attachment*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1, 2, 4*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

ATTACHMENT TO ADVISORY ACTION

1. Applicant's amendment filed on August 30, 2004 is acknowledged and will be entered. The amendments and arguments have been thoroughly reviewed and considered but they are not found persuasive for the reasons that follow. Accordingly, the rejections under 35 U.S.C. 102(a) and 35 U.S.C. 103(a) are maintained and discussed below.

Applicant's traversal

2. Applicant traverses the rejection on the following grounds: Firstly, Applicant request that the finality of the rejections of claims 1, 2 and 4 in the present Office Action be withdrawn, as being premature. Applicant cites section of MPEP 706.07(a). Applicant states that the Office action rejects claims 1, 2 and 4 of the present application on three new grounds. Applicant states that one of the grounds, a rejection of claim 4 for indefiniteness, under 34 U.S.C. 112, second paragraph, was necessitated by an amendment made by Applicants in response to the preceding Office Action. Applicant asserts that neither the other two new rejections set forth in the Office action were necessitated by any amendments made by Applicants, rejection under 35 USC 103(a) over a combination of previously cited reference and an reference not previously cited by the Examiner. Applicant states that line 5 was amended by Applicants in response to the preceding Office Action to stated that the "secreted soluble recombinant calcium channel alpha-2 delta-1 subunit polypeptide is "selected from the group consisting of SEQ ID NO: 13, 14 and 15". Applicant assert that since that same claim language was already in the claims, as originally filed, amendment of claim 1 to incorporate that particular language could not have necessitated the introduction of new grounds for rejection. Applicant also note that the one prior art reference cited for the first time in the present Office action,

Harpold et al., was introduced in an information disclosure state filed prior to issuance of the first office on the merits in accordance with 37 CFR 1.97(b)(3). Applicant states that thus it cannot be said that the reference was introduced so late into prosecution that it would be proper to base a new grounds for rejection in a final Office action. Finally, Applicant concludes that the finality of the rejection of claims 1, 2 and 4 of the present application be withdrawn.

Examiner's Response

3. The arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons that follows: The Examiner acknowledges Applicant's arguments and asserts that the finality of the present Office action is deemed proper because the amended to claim 1 was based on a Markush-type claim (claim 3). MPEP 803.02 discloses the practice regarding examination of Markush-type claims. MPEP 803.02 states that a Markush-type claim can include independent and distinct invention. [I]n applications containing claimed of that nature, the examiner may or may not require a provisional election of a single species prior to examination on the merits. If a Markush-type claim is not allowable over the prior art, examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration. If on the examination the elected species is found to be anticipated or render obvious by prior art, the Markush type claim and claims to the elected species shall be rejected, and claims to the nonelected species would be held withdrawn from further consideration. As in the prevailing practice, a second action on the rejected claims would be made final. On the other hand, should no prior art be found that anticipates or render obvious the elected species, the search of the Markush-type claim will be extended. If prior is then found that anticipates or

renders obvious the Markush-type claim with respect to a non-elected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all non-elected species. Should Applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or render obvious by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extend necessary to determined patentability of the Markush-type claim. **In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final.** (see MPEP 803.02).

In regards to the instant invention, the examiner followed the Markush practice for examination of multiple species. According to MPEP 803.02, finality of the present Office action is deemed proper.

Applicant's traversal

4. Applicant traverses the rejection on the following grounds: Applicant summarizes the examiner's rejections and assert that a prima facie case of obviousness of the subject matter of claims 1 and 4 over Brown et al and Harpold et al has not been established. Applicant states that even of the first two criteria for a prima facie case have somehow been established, the third criteria, the requirement that there be a reasonable expectation of success, has not bee met. Applicant states that Brown et al not only fails to teach a method for the screening of ligands which binds to alpha-2-delta-1, using a soluble recombinant calcium channel alpha-2 delta-1

subunit polypeptide selected from the group consisting of SEQ Id NO: 13-15, as noted in the Office Action; it demonstrates that one of ordinary skill in the art would have expected to encounter may unsuitable or even-nonfunctional polypeptides in a search for substrates suitable for use in an alpha-2-delta-1, a ligand screening method, much less the screening method of claim 1. Applicant states that in fact Brown et al produced 10 peptides of a calcium channel protein, deletion mutants, A-I and N, which are entirely inactive. Applicant asserts that Brown et al provides a calcium channel peptide with ligand binding ability, but which has the acknowledged disadvantage that it is heterogeneous in solubility and purity by a degree of 50% and as such is unsuitable for use in any such ligand-binding assay.

Applicant contends that Harpold et al discloses SEQ Id NO: 11, a 3600 base pair sequence of human genomic DNA encoding for Alpha2 subunits of a calcium channel and goes on to describe the functional characteristics of active peptide fragments of that and other polypeptides encoded by other genomic DNA sequences discloses therein. Applicant contends that Harpold et al provides no path to a solution or indication that any reasonable certainty of success of identifying or making such a peptide. Applicant contends that as noted above, the office actions states that the polypeptide encoded by SEQ ID NO: 11 comprises the polypeptides SEQ ID NOS: 13-15 of claim 1 of the present application. Applicant states that Harpold et al fails to teach or suggest how one could identify or make any of these three particular polypeptides, with any reasonable expectation of success. Finally Applicant concludes that given the level of uncertainty in identifying polypeptides suitable for use in assays demonstrated by Brown et al and the failure of Harpold et al to teach or suggest the polypeptides used in the method of claim 1 of the present invention, Applicant respectfully request that the rejection be

withdrawn. Applicant notes that the rejection of claim 2 should be withdrawn for the reasons made or record above. Applicant asserts that the prior art of Holland et al do not provide the teaching not found in Brown et al and Harpold et al.

Examiner's Response

1. 5. All of the amendments and arguments have been thoroughly reviewed and considered but they are not found persuasive for the reasons that follow: In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, as noted in the prior Office action, the Brown et al reference teaches all of the limitations of claim 1 accepted for the polypeptides recited in SEQ ID NOS: 13, 14, and 15. This limitation is found in the secondary teaching of Harpold et al. Harpold teaches a sequence comprising the polypeptide sequences of SEQ ID NOS: 13, 14 and 15 (SEQ Id NO: 11). Harpold further provides motivation for selecting polypeptide sequences derived from the larger sequence and using them in screening assays such as that taught by Brown et al (see previous Office action).

2. In regards to Applicant's arguments concerning some unsuitable or non-functional polypeptides taught in the Brown et al reference, the Examiner does not understand the relevance of the argument because Brown discloses some polypeptides that are functional and suitable in the screening method. Additionally, there is no recitation in the claims that would exclude a non-functional, inactive or unsuitable polypeptide from being screened by the method. In regards to Applicant's arguments concerning the solubility and purity of the calcium channel

peptide of Brown et al, again the Examiner does not recognize the relevance of the arguments because there is no recitation in the claims that suggest the importance of the solubility and purity of the calcium channel peptide. In fact, the claims do not require a degree of purity of the calcium channel peptides or homogeneous sample. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to Applicant arguments that Harpold et al fails to teach or suggest how one could identify or make any of those three particular polypeptides with any reasonable expectation of success, the Examiner respectfully disagree. Specifically, the reference teaches a sequence with 100% identity to the sequences of SEQ ID NOS: 13-15 (SEQ ID NO: 40). Harpold et al further teaches that the sequence can be fragmented or modified in to smaller peptides that have the same function and may include minor variations in sequence that do not alter the activity of the peptide. The reference further teaches either the full-length calcium channel subunit encoding DNA or fragments thereof can be used in various assay systems, such as ligand screening assays. Therefore, given the teaching of Harpold et al., one of ordinary skill in the art at the time of the claimed invention would have been motivated to utilize the full-length sequence or fragments thereof of the sequence of Harpold et al with a reasonable expectation of success in the ligand screening method of Brown et al. A reasonable expectation of success has been established by Harpold et al in that Harpold et al specifically teach that any fragment or modified peptide of the larger sequences can be utilized in various assay systems as long as the function of the peptide or fragment thereof is maintained. Applicant's arguments are not sufficient to overcome the prior art rejections under 35 USC 103(a). Accordingly, the

rejections directed to claims 1, 2 and 4 are maintained. It is noted that the rejection of claim 2 further comprising the reference of Holland et al is maintained for the reasons discussed above.

CYNTHIA WILDER
PATENT EXAMINER
10/19/2004

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600